REMARKS

I. Claim Status.

Claims 2-11 and 13-36 are pending in the application. Claims 2-6, 8-11 and 13-28 are withdrawn from consideration. Claims 7 and 29-36 are rejected under 35 USC 103(a).

II. Claim Amendments

Claims 7, 9, 11 and 22 are amended, Claims 13-21 are canceled, and new Claims 37-44 are added in the present communication.

Support the amendments to claims 7, 9, 11 and 22 can be found in original claim 1 and throughout the specification, e.g., on page 6 line 7 to page 7 line 7 and page 13 lines 11-15.

Support for new claim 37 can be found e.g., on page 13 lines 11-15.

Support for new claim 38 can be found e.g., on page 19, line 3, page 20, line4, page 22 line24 and page 30 line 22.

Support for new claim 39 can be found, e.g., on page 5 lines 8-9.

Support for new claim 40 can be found, e.g., on page 6 lines 15-17.

Support for new claim 41 can be found, e.g., on page 7 lines 5-6.

Support for new claim 42 can be found, e.g., on page 7 lines 6-7.

Support for new claim 43 can be found, e.g., on page 6 line 24 to page 7 line2 and pages 18-19.

Support for new claim 44 can be found, e.g., on pages 18-19.

Accordingly, the amended and new claims do no not introduce new matter. Applicants respectfully request entry and consideration of the amended and new claims.

III. The Rejection Under 35 USC § 103.

The Office has rejected Claim 7 and 29-36 under 35 USC § 103(a) as being unpatentable over McDevitt et al. (US 6,680,206) in view of Van den Engh et al. (US 5,747,349) for the

reasons stated in numbered paragraphs 6-8 of the Office Action. As a preliminary matter, Applicants respectfully request the Examiner read the entirety of Applicants remarks before concluding that the references are being attacked individually. (See, e.g., Response to Argument, paragraph 8 of the Office Action.) Moreover, Applicant respectfully submit Examiner has provided no reasons rejecting Claims 29-36 and merely restates previous arguments for rejecting Claim 7. Accordingly, Examiner has not made a *prima facie* case of obviousness with respect to Claims 29-36.

Under the Office's policy of compact prosecution, each claim should be reviewed for compliance with every statutory requirement for patentability in the initial review of the application, even if one or more claims are found to be deficient with respect to some statutory requirement. (MPEP §707.07(g). It is submitted that the present application is not sufficiently informal, does not present an undue multiplicity of claims, or exhibit a misjoinder of inventions, so as to reasonably preclude a complete action on the merits. Thus, it is submitted that the Office's failure constitutes a failure to expeditiously provide the information necessary to resolve issues related to patentability that prevents the Applicant from, for example, presenting appropriate patentability arguments and/or rebuttal evidence. (See The Official Gazette Notice of November 7, 2003). Additionally, it is submitted that the Office's failure needlessly encourages piecemeal prosecution, which is to be avoided as much as possible. (MPEP §707.07(g)). Accordingly, in the event that the Office maintains the rejection of any of the dependent claims, Applicant respectfully requests, in the interests of compact prosecution, that the Office apply art against each feature of each rejected dependent claim, on the record, and with specificity sufficient to support a *prima facie* case of obviousness.

Claim 7 is amended in the present application to further distinguish the claimed invention over the cited references. Accordingly, Applicants respectfully traverse the rejection and request reconsideration based on the following remarks.

McDevitt et al. (US 6,680,206) and Van den Engh et al. (US 5,747,349) do not teach all the claimed limitations

McDevitt et al. discloses a system of particles formed in an ordered array (Col. 4, line 26-

28; col. 8, lines 2-3, 17-19, and 41-47), which can utilize a plurality of sensitive particles for identification of multiple analytes. Van den Engh et al. teaches "reporter beads for chemical analysis of fluid bulk properties." (column 3 lines 28-30). However, McDevitt et al. and Van den Engh et al. fail to disclose:

- ion-sensor particles having associated therewith a target ionophore (Claim 7); any of the specific target ionophores set forth in Claim 43; or any combination of target ionophore and fluorescent indicator as set forth in Claims 40-42.
- any target metabolite or antigen analogues having a fluorescent label (Claim 33)
- any second reporter antibody labeled with a fluorescent label (Claim 35)

There is no teaching, suggestion, or motivation to combine different classes of sensor particles in a common reagent mixture found either in McDevitt et al. or Van den Engh et al or in the knowledge generally available to one of ordinary skill in the art

Applicants respectfully submit that McDevitt et al. is devoid of any teaching to combine sensor particles in a reagent mixture. Van den Engh et al. does not disclose a reagent mixture of different classes of sensor particles, the reagent mixture comprising sensor particles selected from each of the classes (a), ion-sensor particles; class (b), metabolite-sensor particles, and class (d) antigen- or antibody-sensor particles. Although the Van den Engh et al. may teach the desirability of combining beads with different reporter molecules, the reference is devoid any teaching that suggests mixing immunoassay reporter beads with "reporter beads for chemical analysis of fluid bulk properties." (column 3 lines 28-30).

As noted above, Van den Engh et al. does not explicitly teach a reagent mixture or "cocktail" which includes different classes of particles or "beads" tailored to quantitatively detect specific analytes, wherein at least one bead from each of the classes directed to measurement of enzymes, antibodies or antigens, and/or nucleotide sequences. Further, Van den Engh et al. specifically teaches away from including antigen or antibody sensors with other reporter beads for the chemical analysis of fluid bulk analytes.. Van den Engh et al. teaches in the Background section that "antigens in the fluid can be detected by the aggregation of antibody coated fluorescent beads." (Van der Engh, col. 1, lines 62-64). However, the reference then teaches the

following in the Detailed Description of the Invention:

> In further contrast, the reporter beads of this invention ***are not required to have*** an immunoreagent, such as a ligand, antiligand, ***antigen or antibody***, on the surface in combination with the reporter molecules." (Col. 3, lines 60-64, emphasis added).

Further,

> The interaction ***need not be a ligand/antiligand or antigen/antibody reaction***. The interaction preferably does not lead to an aggregate with other particles and, in particular, does not create an aggregate containing a plurality of reporter beads. (Col. 4, lines 13-18).

When the Van den Engh et al. reference is taken as whole, it is apparent that combining sensor particles for general chemistry analytes, such electrolytes and/or small metabolites, with enzymes, antibodies, antigens and polynucleotide sequences, is not contemplated or considered desirable. Thus, neither reference suggest combining sensor particles for the enzyme, DNA, antigen or antibody assays of McDevitt et al. with sensor particles for the general chemistry assays of Van den Engh et al. in a common reagent mixture.

The combination of McDevitt et al. and Van den Engh et al. fails to provide a reasonable expectation of success.

A person of skill in the art confronted with the technical problem of providing an assay method that enables the detection of multiple analytes, would recognize the technical difficulties inherent in combining assays for general chemistry analytes, such as ions and metabolites with assays for biological analytes, such antibodies, antigens, enzymes or nucleotide sequence, in a common reagent mixture. All of the particles in Applicants' claimed mixture are subjected to a common aqueous buffer that allows for reactions between particles that have diffusible reaction products. The common reaction environment means that assays on some particles are suboptimized in order to allow effective assay on other particles. For example, a first assay particle may have optimal sensitivity at alkaline pH. This pH, however, destroys the responsivity of particles assaying for potassium, which require that the indicator be protonated to produce the detectable ion exchange. This expectation of interference and sub-optimal responsivity would lead those skilled in the field away from a reagent mixture comprising

different classes of sensor particles having a common aqueous buffer. However, as described in the specification, Applicants designed an effective assay for multiple particles in suspension, which balances the competing needs of different assays. That nonsimilar sensors can be combined in a single mixture and retain functionality is further evidence of the unexpected nature the present invention.

CONCLUSION

Neither the McDevitt et al. nor the Van der Engh et al. reference teach or suggest a mixture of sensor particles suitable for flow cytometry, which includes ion-, metabolite- and antigen/antibody sensors, nor do the combined references provide a reasonable expectation of success for the utility of such a reagent mixture. Moreover, the combined references fail to teach all the limitations of the independent and dependent claims. Accordingly, the claimed combination is not obvious and Applicants request withdrawal of the rejection under 35 U.S.C. § 103 as well as allowance the pending claims.

The Applicant believes that all pending claims are in condition for allowance and such action is earnestly requested. If the present amendments and remarks do not place the Application in condition for allowance, the Examiner is encouraged to contact the undersigned directly if there are any issues that can be resolved by telephone with the Applicants representative.

A fee of $120 for a one month extension of time is believed due with this communication. The Commissioner is authorized to charge this fee and any other fee believed due to Deposit Account No. 19-2090.

Respectfully Submitted,
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